REMARKS

Claims 1-51 are pending in the application. In a non-final Office Action mailed April 1, 2003, claims 24-51 were allowed, claims 1-4, 7, 8, 13-16, 18, and 19 were rejected under 35 U.S.C. 103(a) as being unpatentable over Smith et al. (U.S. Patent No. 6,027,945), in view of Schneider et al. (U.S. Patent No. 4,925,818), and claims 5, 6, 9-12, 17, and 20-23 were objected to as depending from a rejected claim. The rejection of claims 1-4, 7, 8, 13-16, 18, and 19 under 35 U.S.C. 102(e) as being anticipated by Smith et al. made in the previous Office Action mailed November 25, 2002 was withdrawn.

Applicants have amended independent claim 1, from which claims 2-4, 7, and 8 depend, and independent claim 13, from which claims 14-16, 18, and 19 depend, to clarify that in the method as claimed, the silanized matrix is contacted with a solution comprising disrupted biological material, target nucleic acid material, and chaotropic salt at a concentration sufficient to promote selective adsorption of the disrupted biological material to the matrix, to form a complex between the silanized silica matrix and the disrupted biological material. Support for the amendment can be found, for example, at page 5, lines 18-21, and at page 11, lines 1-5.

In view of the amendments above and the arguments below, Applicants request reconsideration on the merits and allowance of the claims.

Rejection of claims 1-4, 7, 8, 13-16, 18, and 19 under 35 U.S.C. 103(a)

Claims 1-4, 7, 8, 13-16, 18, and 19 were rejected under 35 U.S.C. 102(e) as being unpatentable over Smith *et al.* (U.S. Patent No. 6,027,945) in view of Schneider et al. (U.S. Patent No. 4,925,818). Independent claims 1 and 13, as amended, are reproduced below.

1. A method of clearing a solution of disrupted biological material, according to steps comprising:

(a) providing a first silanized silica matrix, comprising a silica solid phase with a plurality of silane ligands covalently attached thereto, wherein each of the plurality of ligands has a neutral charge in a first solution; and

(b) combining the first silanized silica matrix with the first solution, comprising a disrupted biological material, a target nucleic acid material, and a chaotropic salt at a concentration sufficient to promote selective adsorption of the disrupted biological material

to the matrix, thereby forming a first complex between the silanized silica matrix and the disrupted biological material.

13. A method of clearing a solution of disrupted biological material, according to steps comprising:

(a) providing a first silanized silica magnetic particle comprising a silica magnetic particle with a plurality of silane ligands covalently attached thereto;

(b) combining the first silanized silica magnetic particle with a first solution, comprising a disrupted biological material, a target nucleic acid, and a chaotropic salt concentration sufficiently high to promote selective adsorption of the disrupted biological material to the silanized silica magnetic particle, thereby forming a first complex between the silanized silica matrix and the disrupted biological material;

(c) separating the first complex from the first solution, thereby forming a cleared solution.

According to the Examiner, Smith et al. teaches methods of isolating biological target materials using silica magnetic particles including nucleic acids such as DNA or RNA using silica magnetic particles by forming a mixture comprising a medium including plasmid DNA, siliceous-oxide coated magnetic particle, and a chaotropic salt in a concentration sufficiently high to cause the *target* material to adhere to the silica magnetic particles. Schneider et al. was characterized as disclosing a ligand specific to a bioactive substance to be purified, the ligand fixed to a mineral particulate carrier such as SiO_2 by a connecting silane linker. The carrier is contacted with an aqueous extract containing the bioactive substances, which are specifically fixed to the carrier. The carrier is then separated and the *desired* bioactive substance is isolated by desorption. (emphasis added)

In contrast, claims 1-4, 7, 8, 13-16, 18, and 19 are drawn to methods of clearing a solution of disrupted biological material (defined in the specification at page 8, lines 3-6 as referring to material other than target nucleic acid, released when biological materials, such as bacterial cells, mammalian tissue, blood cells, or plant material, are disrupted, and may include proteins, lipids, cellular debris, and non-target nucleic acids). In the method, the silanized matrix is contacted with a first solution comprising the disrupted biological material, target nucleic acid, and chaotropic salt in a concentration sufficient to promote selective adsorption of the disrupted biological material to the silica matrix to form a complex between the silica matrix and the disrupted biological target material. In contrast to Smith et al. or Schneider et al., which teach binding of the target material or the desired bioactive

substance to the silica, the present invention claims selective adsorption of the disrupted biological material from a solution comprising the disrupted biological material and target nucleic acid to form a complex between the silica matrix and the disrupted biological material.

Smith et al. discloses that non-derivatized silica (i.e., silica that is not silanized) will bind to nucleic acids under chaotropic conditions. In contrast, in the method of claims 1-4, 7, 8, 13-16, 18, and 19, under chaotropic conditions, silanized silica forms preferentially adsorbs to disrupted biological material (e.g., cell debris) to form a solution cleared of disrupted biological material. In other words, under chaotropic conditions, the non-silanized silica particles of Smith et al. bind to target nucleic acids, but do not selectively adsorb disrupted biological material to form a solution cleared of disrupted biological material.

Schneider et al. does not cure the deficiencies of the primary reference. Schneider et al. uses silane as a linker to attach a ligand (e.g., bacitracin, concanavalin A lectin, or an antibody) to silica, which ligand is used to specifically bind the desired bioactive substance to the silica. In contrast to the present invention, in which undesired, disrupted biological material is removed from a solution comprising disrupted biological material, target nucleic acid, and a chaotropic agent in a concentration sufficient to promote selective adsorption of the disrupted biological material to the silanized silica matrix, leaving the desired target nucleic acids in solution, Schneider et al. teaches specific binding of the target material to the ligand. In Schneider et al., the ligand bound to the silanized silica is not provided as disrupted biological material in a solution comprising disrupted biological material and a target nucleic acid and selectively adsorbed to the silanized silica. Rather, a relatively pure ligand is reacted with a suitable silane (i.e., a silane having a reactive group) to form a silica-ligand system for subsequent use in the isolation of a desired bioactive substance (i.e., target molecule) through specific interaction of the target molecule with the attached ligand.

The Examiner indicated that the motivation to combine Smith et al. and Schneider et al. is provided by the disadvantages of the prior art that Schneider et al. purports to overcome. However, the passages cited by the Examiner relate to the advantages of using non-porous submicronized silica relative to using porous silica. Applicants respectfully submit that the alleged advantages disclosed by Schneider et al. simply would not provide motivation to make the claimed invention, and wish to emphasize that the instantly claimed methods are not limited to use with a silica matrix having a particular porosity or to use with non-porous silica.

Applicants respectfully submit that the art of record does not combine to teach all of the claim limitations, and as such, a prima facie case of obviousness has not been established. Specifically, neither reference teaches making a lysate cleared of disrupted biological material by contacting a silanized silica matrix with a solution containing the disrupted biological material, a target nucleic acid, and a chaotrope in a concentration sufficient to promote selective adsorption of the disrupted biological material to the silica matrix. In view of the foregoing, Applicants respectfully request that the rejection be withdrawn and claims 1-51 allowed.

This response is accompanied by a check to cover the large entity fee associated with the two-month extension of time. No other fee is believed due in connection with this response. However, if an additional fee is owed, please charge such fee to Deposit Account No. 50-0842.

Respectfully submitted,

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